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SEA SPHINGOMYELINASE

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                38   FILE [redacted]PINDEX
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     18 JAN 2001
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L3              66 S L2 AND (INHIBITO? OR AGENT)
L4              39 DUP REM L3 (27 DUPLICATES REMOVED)
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L4 ANSWER 14 OF 39 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:479640 CAPLUS
DOCUMENT NUMBER: 129:91437
TITLE: Cloning and expression of human neutral **sphingomyelinase** cDNA and diagnosis and treatment of diseases related to this enzyme
INVENTOR(S): Chatterjee, Subroto
PATENT ASSIGNEE(S): The Johns Hopkins University, USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9828445	A1	19980702	WO 1997-US24051	19971223
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5919687	A	19990706	US 1996-774104	19961224
AU 9858093	A1	19980717	AU 1998-58093	19971223
EP 948651	A1	19991013	EP 1997-954272	19971223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRIORITY APPLN. INFO.:			US 1996-774104	19961224
			WO 1997-US24051	19971223

AB Human neutral **sphingomyelinase** (N-SMase) and nucleic acids encoding N-SMase as well as the cloning/expression of N-SMase nucleic acid and the vectors and recombinant cells used in this process are disclosed. Methods to identify compds. useful in the diagnosis or treatment of N-SMase-related **disorders** and methods for treating such **disorders** are claimed. Thus, human kidney N-SMase cDNA was cloned and expressed. Expression of this cDNA in aortic smooth muscle cells increased apoptosis in these cells.

L4 ANSWER 20 OF 39 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:340296 CAPLUS
DOCUMENT NUMBER: 125:8705
TITLE: **Sphingomyelinase**-inhibiting F 11263 and its manufacture with Acremonium species
INVENTOR(S): Ogura, Yoko; Nara, Futoshi; Hosoya, Takeshi
PATENT ASSIGNEE(S): Sankyo Co, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08053387	A2	19960227	JP 1994-189722	19940812

AB The title compd. (I), useful for treatment of diabetes mellitus, arteriosclerosis, osteoporosis, thrombosis, etc., is manufd. by I-producing Acremonium sp., e.g. Acremonium sp. SANK 11894. Acremonium sp. SANK 11894 was shake-cultured in a medium contg. glycerol, potato, yeast ext., and malt ext. at 23.degree. for 7 days to produce 199.9 mg I, which inhibited **sphingomyelinase** with IC50 0.8 .mu.g/mL. The physiol. and morphol. characteristics of the Acremonium sp. SANK 11894 and

L4 ANSWER 21 OF 39 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:837561 CAPLUS
DOCUMENT NUMBER: 123:254697
TITLE: **Sphingomyelinase inhibitor** F-10463a manufacture with Dasyscyphus
INVENTOR(S): Ogita, Takeshi; Nara, Futoshi; Tanzawa, Kazuhiko; Hosoya, Tsuyoshi; Furuya, Kouhei
PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9518119	A1	19950706	WO 1994-JP2202	19941226
W: AU, CA, CN, CZ, FI, HU, KR, NO, NZ, RU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
JP 07233158	A2	19950905	JP 1994-317868	19941221
AU 9512805	A1	19950717	AU 1995-12805	19941226
PRIORITY APPLN. INFO.:			JP 1993-330613	19931227
			WO 1994-JP2202	19941226

AB A novel compd. F-10463a (I), a **sphingomyelinase inhibitor**, is manufd. by culturing D. mollissimus (lasch) Dennis SANK 13892. I is useful as an anti-HIV drug, antidiabetic, antiarteriosclerotic, antiosteoporotic, antithrombotic, anti-inflammatory, immunosuppressant, diuretic, and a preventive or remedy for respiratory disease, thyroid disease, Alzheimer's disease, hepatitis, nephritis, leukemia, and cachexia. The physicochem. characteristics of I and physiol. and morphol. characteristics of D. mollissimus (lasch) Dennis SANK 13892 were given. Shake-culture of the microorganism and isolation of I from the microorganism by extn. and chromatog. were shown.

L4 ANSWER 22 OF 39 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:993035 CAPLUS
DOCUMENT NUMBER: 124:28118
TITLE: Novel hydroquinones, their manufacture with Acremonium, and Acremonium sp. SANK20793
INVENTOR(S): Nara, Futoshi; Ogita, Takeshi; Tanzawa, Kazuhiko; Hosoya, Takeshi; Furuya, Kohei
PATENT ASSIGNEE(S): Sankyo Co, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07258132	A2	19951009	JP 1994-48584	19940318

AB F-11334A1 (e.g. I), F-11334A2 (II), F-11334A3 (III), F-11334B1 (IV), and/or F-11334B2 (V) are manufd. by culturing Acremonium sp. producing I, II, III, IV, and/or V. The hydroquinones are useful as anti-HIV **agents**, antidiabetics, antiarteriosclerotics, antiosteoporotic **agents**, antithrombotics, inflammation **inhibitors**, immunosuppressants, diuretics, and treatment **agents** for respiratory tract diseases, thyroid gland diseases, Alzheimer's disease, hepatitis, nephritis, leukemia, and cachexia. Acremonium sp. SANK20793 was shake-cultured in a medium contg. glycerol, potato, yeast ext., malt ext., and antifoamer for 5 days and shake-cultured in the same medium (100 mL .times. 15) at 23.degree. for 7 days, centrifuged, the cells extd. with acetone, and the ext. was processed to give I 19, II 7, III 23, IV 4.5, and V 10 mg. I inhibited **sphingomyelinase** with IC50 of 38.8 .mu.g/mL. The microbial properties of the Acremonium sp. and the physicochem. properties of the hydroquinones are also given.

L4 ANSWER 37 OF 39 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 8
ACCESSION NUMBER: 81205781 EMBASE
DOCUMENT NUMBER: 1981205781
TITLE: Experimental Niemann-Pick rat: Additional studies on the specificity of the **sphingomyelinase** reduction in rats treated with AY 9944.
AUTHOR: Watanabe K.; Sakuragawa N.; Arima M.
CORPORATE SOURCE: Div. Child Neurol., Nat. Cent. Nerv. Ment. Musc. Disorders,
Ogawa-Higashi Machi, Kodaira, Tokyo, Japan
SOURCE: Brain and Nerve, (1981) 33/6 (585-593).
CODEN: NOTOA6
COUNTRY: Japan
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
029 Clinical Biochemistry
030 Pharmacology
LANGUAGE: Japanese
SUMMARY LANGUAGE: English
AB Niemann-Pick disease, an inherited neurological **disorder**, is characterized biochemically by a deficiency of the lysosomal acid **sphingomyelinase**, which catalyzes the hydrolysis of sphingomyelin to ceramide and phosphorylcholine. Sakuragawa et al. previously described the specific reduction of acid **sphingomyelinase** activities in various tissues and organs of suckling rats which recieved intraperitoneal injection of a hypocholesterolemic **agent**, AY 9944 (trans-1,4-bis[2-chlorobenzylaminomethyl] cyclohexane dihydrochloride). The results of more detailed studies about the specificity of the **sphingomyelinase** reduction caused by AY 9944 are reported.

L4 ANSWER 31 OF 39 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:422018 CAPLUS
DOCUMENT NUMBER: 115:22018
TITLE: Rapid kidney changes resulting from glycosphingolipid depletion by treatment with a glucosyltransferase **inhibitor**
AUTHOR(S): Shukla, Girja S.; Shukla, Arti; Inokuchi, Jinichi; Radin, Norman S.
CORPORATE SOURCE: Ment. Health Res. Inst., Univ. Michigan, Ann Arbor, MI, USA
SOURCE: Biochim. Biophys. Acta (1991), 1083(1), 101-8
CODEN: BBACAQ; ISSN: 0006-3002
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The ceramide analog, D-threo-1-phenyl-2-decanoylamino-3-morpholino-1-propanol, inhibits the glycosylation of ceramide and thus, by virtue of the normal catabolism of the higher glycosphingolipids, leads to a general depletion of cellular glycolipids. In a previous study with chronic administration of this **inhibitor** in mice, it was found that the kidneys and liver, particularly the former, grew more poorly than the organs of control mice. This study shows that the **inhibitor** produces rapid decreases in glycolipid concn. in kidneys which are maintained for at least 5 days without noticeable harm. The changes were enhanced by inclusion of L-cycloserine in the injection scheme. Cycloserine blocks ketosphinganine synthase and thus slows the synthesis of all sphingolipids. However, sphingomyelin levels did not drop significantly in this study. The glucosyltransferase **inhibitor** also produced a small decrease in kidney .beta.-D-glucuronidase and distinct increases in the levels of glucocerebrosidase, galactocerebrosidase and **sphingomyelinase**. It also produced a small but distinct decrease in the level of glucosyltransferase, after a delay of a few hours, possibly because the **inhibitor** was metabolized to a covalently inactivating product. Comparison of kidney, liver and brain showed that the kidney was more sensitive to the action of the morpholino **inhibitor**.

L4 ANSWER 30 OF 39 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1992:14089 BIOSIS
DOCUMENT NUMBER: BR42:1789
TITLE: **SPHINGOMYELINASE** FIBROBLAST ACTIVITY AND PSYCHOACTIVE DRUGS.
AUTHOR(S): LEJOYEUX M; MAZIERE J C; MORA L; AUCLAIR M; MAZIERE C
CORPORATE SOURCE: DEP. PSYCHIATRY, HOP. LOUIS MOURIE, 92700 COLOMBES, FR.
SOURCE: Biol. Psychiatry, (1991) 30 (8), 841-843.
CODEN: BIPCBF. ISSN: 0006-3223.
FILE SEGMENT: BR; OLD
LANGUAGE: English

L4 ANSWER 29 OF 39 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1992:266497 BIOSIS
DOCUMENT NUMBER: BR42:125447
TITLE: REMOVAL OF LIPOPROTEIN FRACTION FROM CULTURE MEDIA CORRECTS
THE REDUCTION OF ACID **SPHINGOMYELINASE** ACTIVITY INDUCED BY AY9944.
AUTHOR(S): YOSHIKAWA H; SAKURAGAWA N
CORPORATE SOURCE: DIV. INHERITED METABOLIC DISORDERS, NATL. INST. NEUROSCI., NATL. CENT. NEUROL. PSYCHIATRY, 4-1-1 OGAWAHIGASHI-CHO, KODAIRA, TOKYO 187, JPN.
SOURCE: J. Inherited Metab. Dis., (1992) 15 (1), 155-156.
CODEN: JIMDDP. ISSN: 0141-8955.
FILE SEGMENT: BR; OLD
LANGUAGE: English

L4 ANSWER 39 OF 39 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1978:134237 CAPLUS
DOCUMENT NUMBER: 88:134237
TITLE: Experimental model of Niemann-Pick disease: **sphingomyelinase** reduction induced by AY-9944
AUTHOR(S): Sakuragawa, Norio
CORPORATE SOURCE: Brain Res. Inst., Niigata Univ., Niigata, Japan
SOURCE: No To Hattatsu (1978), 10(1), 2-9
CODEN: NTHAA7; ISSN: 0029-0831
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB AY-9944 administered i.p. into rats decreased **sphingomyelinase** activity and increased sphingomyelin C concn. in the liver, indicating that AY-9944 is an effective **agent** to induce Niemann-Pick disease, a hereditary **disorder** in fat metab.

Brain Res Bull 1983 May;10(5):603-6

Stimulation of neutral, magnesium-stimulated sphingomyelinase activity in the neurohypophysis of the rat by hypertonic saline ingestion.

Guy NC, Clarke JT, Spence MW, Cook HW

Neutral, magnesium-stimulated sphingomyelinase and acid sphingomyelinase activities in the neurohypophysis, adenohypophysis and cerebrum of rats given 2.25% NaCl drinking water for 7 or 14 days were compared with the same enzyme activities in the tissues of control animals allowed free access to distilled drinking water. Neutral sphingomyelinase activity in the neurohypophysis was significantly increased in both experimental groups (7-day, 85.2 +/- 8.4 units/mg protein; 14-day, 110.1 +/- 14.8 units/mg; control, 61.4 +/- 5.5 units/mg). Acid sphingomyelinase activity was significantly but only transiently increased in the tissue (7-day, 73.2 +/- 3.4 units/mg; 14-day, 66.3 +/- 7.5 units/mg; control, 54.3 +/- 2.8 units). Enzyme activities in adenohypophysis and cerebrum of the experimental animals were not significantly different from those of controls. The results suggest a specific role for neutral, Mg2+-stimulated sphinomyelinase in neurosecretion.

PMID: 6307490, UI: 83258633

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☐ Uchida R, et al. [See Related Articles]

Alutenusin, a specific neutral sphingomyelinase inhibitor, produced by Penicillium sp. FO-7436.
J Antibiot (Tokyo). 1999 Jun;52(6):572-4. No abstract available.
PMID: 10470682; UI: 99397283.

☐ Nara F, et al. [See Related Articles]

Biological activities of scyphostatin, a neutral sphingomyelinase inhibitor from a discomycete, Trichopeziza mollissima.
J Antibiot (Tokyo). 1999 Jun;52(6):531-5.
PMID: 10470676; UI: 99397277.

☐ Nara F, et al. [See Related Articles]

Scyphostatin, a neutral sphingomyelinase inhibitor from a discomycete, Trichopeziza mollissima: taxonomy of the producing organism, fermentation, isolation, and physico-chemical properties.
J Antibiot (Tokyo). 1999 Jun;52(6):525-30.
PMID: 10470675; UI: 99397276.

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Biochem Biophys Res Commun 1990 Mar 16;167(2):607-13

Dexamethasone increases neutral sphingomyelinase activity and sphingosine levels in 3T3-L1 fibroblasts.

Ramachandran CK, Murray DK, Nelson DH

Department of Medicine, University of Utah School of Medicine, Salt Lake City 84132.

The activity of neutral sphingomyelinase (EC 3.1.4.12) in a plasma membrane enriched fraction was found to be increased in dexamethasone treated cells. The elevation of sphingomyelinase activity was blocked by cycloheximide indicating that protein synthesis was required for the steroid action. Ceramidase (EC3.5.1.23) activity was unaffected by the dexamethasone treatment. Levels of sphingosine in 3T3-L1 Cells were also increased after treatment with 10(-7) M dexamethasone for 2 and 4 hours.

PMID: 2157410, UI: 90211236

Biochim Biophys Acta 1996 Mar 29;1300(1):42-8

Identification of an alkaline sphingomyelinase activity in human bile.

Nyberg L, Duan RD, Axelson J, Nilsson A

Swedish Dairies' Association, Lund.

The hydrolysis of sphingomyelin has been found to generate important signals regulating cell proliferation, differentiation and apoptosis. However, the enzymes responsible for digestion of dietary sphingomyelin have not been well documented. This study demonstrates the occurrence of a sphingomyelinase (SMase) in both human hepatic bile and gallbladder bile. The enzyme was equally found in both bacteria negative and positive bile samples and in samples obtained from patients with or without gallbladder diseases. A bacteria-free gallbladder bile was used for characterization. It was found that bile SMase hydrolyzed sphingomyelin to phosphorylcholine and ceramide with negligible activity against either phosphatidylcholine or p-nitrophenyl phosphate. The enzyme preferred an alkaline condition and the optimal pH was 9. The activity of this alkaline SMase was bile salt dependent and was fully activated by 4-6 mM bile salts. Triton X-100, the non-ionic detergent did not activate bile SMase. Ca2+ and Mg2+ ions had no significant effect at optimal bile salt concentration. The molecular mass of this enzyme was about 85 kDa as measured by Sephadex G200 gel chromatography. In conclusion, we demonstrated a SMase in bile which differs markedly from the known acid and neutral SMase. Its potential important roles in sphingomyelin digestion and gallbladder diseases require further investigation.

PMID: 8608160, UI: 96185196